

What is claimed:

- 1        1.     A composition comprising a curable admixture of a bone substitute and a  
2     crosslinkable prepolymer, wherein the crosslinkable prepolymer comprises an anhydride of  
3                (i)     a monomer or oligomer of a diacid or multifunctional acid and  
4                (ii)    a carboxylic acid molecule which includes a crosslinkable group, wherein  
5     the crosslinkable group is an unsaturated hydrocarbon moiety.
  
- 1        2.     The composition of claim 1 further comprising an initiator.
  
- 1        3.     The composition of claim 2, wherein the initiator is a photoinitiator.
  
- 1        4.     The composition of claim 1 wherein the crosslinkable prepolymer is linear with  
2     an unsaturated hydrocarbon moiety at each terminus.
  
- 1        5.     The composition of claim 1 wherein the crosslinkable prepolymer comprises a  
2     dianhydride of a dicarboxylic acid monomer or oligomer and a carboxylic acid molecule  
3     comprising an unsaturated moiety.
  
- 1        6.     The composition of claim 5, wherein the crosslinkable prepolymer comprises a  
2     methacrylic acid dianhydride of a monomer or oligomer of a diacid selected from the group  
3     consisting of sebacic acid and 1,3-bis(p-carboxyphenoxy)-alkane.
  
- 1        7.     The composition of claim 6, wherein the 1,3-bis(p-carboxyphenoxy)-alkane is  
2     1,3-bis(p-carboxyphenoxy)-propane.
  
- 1        8.     The composition of claim 1, wherein the crosslinkable prepolymer further  
2     comprises a second anhydride of

- (i) a monomer or oligomer of a diacid or multifunctional acid and
- (ii) a carboxylic acid molecule which includes a crosslinkable group, wherein  
the group is an unsaturated hydrocarbon moiety, and  
in the second anhydride is different from the first anhydride.

9. The composition of claim 8, wherein the first anhydride is a methacrylic acid dianhydride of a monomer or oligomer of sebacic acid; and the second anhydride is a methacrylic acid dianhydride of a monomer or oligomer of 1,3-bis(p-carboxyphenoxy)-alkane.

1 10. The composition of claim 8, wherein the ratio of the first anhydride to the second  
2 anhydride is from about 1:20 to about 20:1.

1 11. The composition of claim 9, wherein the ratio of the first anhydride to the second  
2 anhydride is from about 1:5 to about 5:1.

1                   12. The composition of claim 9, wherein the ratio of the first anhydride to the second  
2 anhydride is from about 1:5 to about 1:1.

1                   13. The composition of claim 9, wherein the ratio of the first anhydride to the second  
2 anhydride is from about 1:1 to about 1:5.

1 14. The composition of claim 1, wherein the bone substitute is an autograft, allograft,  
2 xenograft or alloplast or mixture thereof.

15. The composition of claim 14, wherein the alloplast is polymeric.

1                   16.     The composition of claim 1, wherein the bone substitute comprises porous  
2     micron-sized particles, each particle having a core layer of a first biocompatible polymeric

3 material and a coating of a second biocompatible polymeric material surrounding the core layer,  
4 wherein the second polymeric material is hydrophilic and different in composition from the first  
5 polymeric material.

1 17. The composition of claim 16, wherein the diameter of the micron-sized particles  
2 is from about 250 microns to about 900 microns.

1 18. The composition of claim 16, wherein the first polymeric material is  
2 poly(methylmethacrylate).

1 19. The composition of claim 16, wherein the second polymeric material is a  
2 poly(hydroxyethylmethacrylate).

1 20. The composition of claim 16, wherein calcium hydroxide is distributed on the  
2 outer surface of and inside the micron-sized particles.

1 21. The composition of claim 1, wherein the ratio of the bone substitute to the  
2 crosslinkable prepolymer is from about 1:20 to 20:1.

1 22. The composition of claim 21, wherein the ratio of the bone substitute to the  
2 crosslinkable prepolymer is from about 1:2 to 2:1.

1 23. The composition of claim 1, further comprising a therapeutic agent.

1 24. A cured composition comprising a bone substitute and a crosslinked prepolymer,  
2 wherein the prepolymer prior to crosslinking is one or more anhydride(s) of  
3 (i) a monomer or oligomer of a diacid or multifunctional acid and

4 (ii) a carboxylic acid molecule which includes a crosslinkable group, wherein  
5 the crosslinkable group is an unsaturated hydrocarbon moiety.

1           25. The cured composition of claim 24, wherein at least 20% (w/w) of the cured  
2 composition biodegrades in from about 6 to 10 weeks.

1           26. The cured composition of claim 25, wherein at least 50% (w/w) of the cured  
2 composition biodegrades in from about 6 to 10 weeks.

1           27. The cured composition of claim 24, wherein at least 20 % (w/w) of the cured  
2 composition biodegrades in from about 6 to 12 months.

1           28. The cured composition of claim 27, wherein at least 50% (w/w) of the cured  
2 composition biodegrades in from about 6 to 12 months

1 29. A method of promoting bone generation comprising the steps of:

2 (A) applying to an area in need of such promotion a composition comprising a curable

3 admixture of a bone substitute and a crosslinkable prepolymer, wherein the crosslinkable

4 prepolymer comprises an anhydride of

5 (i) a monomer or oligomer of a diacid or multifunctional acid and

6 (ii) a carboxylic acid molecule which includes a crosslinkable group, wherein

7 the crosslinkable group is an unsaturated hydrocarbon moiety; and

8 (B) curing the composition.

1 30. A method of stabilizing a dental implant comprising the step of:

2 at least partially embedding a dental implant into a cured composition wherein the cured  
3 composition is obtained by curing a curable admixture of a bone substitute and a crosslinkable  
4 prepolymer, wherein the crosslinkable prepolymer comprises an anhydride of  
5 (i) a monomer or oligomer of a diacid or multifunctional acid and  
6 (ii) a carboxylic acid molecule which includes a crosslinkable group, wherein  
7 the crosslinkable group is an unsaturated hydrocarbon moiety.

1 31. The method of claim 30, wherein the dental implant is at least partially embedded  
2 into the cured composition by the steps of :

3 (1) planting a dental implant into a bone and/or bone void;  
4 (2) at least partially embedding the dental implant by applying a curable admixture  
5 around the dental implant; and  
6 (3) curing the curable admixture to form the cured composite.

1 32. The method of claim 30, wherein the dental implant is at least partially embedded  
2 into the cured composition by the steps of:

3 (1) at least partially filling a bone void by applying a curable admixture;  
4 (2) curing the curable admixture to form the cured composite; and  
5 (3) planting a dental implant into the bone by at least partially embedding the dental  
6 implant into the cured composite.

1 33. A method of preparing objects of desired shape and size comprising the step of:  
2 curing in a mold a curable admixture of a bone substitute and a crosslinkable prepolymer,  
3 wherein the crosslinkable prepolymer comprises an anhydride of  
4 (i) a monomer or oligomer of a diacid or multifunctional acid and

(ii) a carboxylic acid molecule which includes a crosslinkable group, wherein  
the group is an unsaturated hydrocarbon moiety.

34. A method of drug delivery comprising the steps of:

(A) applying to an area in need of drug delivery a composition comprising a curable

3 admixture of a bone substitute and a crosslinkable prepolymer, and a therapeutic agent,

wherein the crosslinkable prepolymer comprises an anhydride of

(i) a monomer or oligomer of a diacid or multifunctional acid and

(ii) a carboxylic acid molecule which includes a crosslinkable group, wherein the crosslinkable group is an unsaturated hydrocarbon moiety; and

(B) curing the composition.

35. A composition comprising a curable admixture of a polymeric bone substitute and

2 a crosslinkable prepolymer wherein the crosslinkable prepolymer comprises:

(A) a linear polymer selected from the group consisting of linear, hydrophobic

4 biodegradable polymers and linear non-degradable hydrophilic polymers; and

(B) at least one monomer or macromer containing at least one free radical

6 polymerizable group, wherein at least one of the monomers or macromers includes an anhydride  
7 linkage and a polymerizable group selected from the group consisting of acrylate or  
8 methacrylate.

36. The composition of claim 35, further comprising an initiator.

37. The composition of claim 36, wherein the initiator is a photoinitiator.

1           38.     The composition of claim 35, wherein the monomer or macromer contains 1 to  
2     100 repeating units.

1           39.     The composition of claim 35, wherein the linear hydrophobic biodegradable  
2     polymer is formed from one or more units selected from the group consisting of polyanhydrides,  
3     polyorthoesters, polyhydroxy acids, polydioxanones, polycarbonates, and polyaminocarbonates.

1           40.     The composition of claim 35, wherein the linear non-degradable hydrophilic  
2     polymer is formed from one or more units selected from the group consisting of poly(ethylene  
3     glycol), poly(ethylene oxide), partially or fully hydrolyzed poly(vinyl alcohol), poly(ethylene  
4     oxide)-co-poly(propylene oxide) block copolymers (poloxamers and meroxapols) and  
5     poloxamines.

1           41.     The composition of claim 35 wherein the polymeric bone substitute comprises  
2     porous micron-sized particles, each particle having a core layer of a first biocompatible  
3     polymeric material and a coating of a second biocompatible polymeric material surrounding the  
4     core layer, wherein the second polymeric material is hydrophilic and different in composition  
5     from the first polymeric material.

1           42.     The composition of claim 41, wherein the diameter of the micron-sized particles  
2     is from about 250 microns to about 900 microns.

1           43.     The composition of claim 41, wherein the polymeric bone substitute further  
2     comprising a quantity of calcium hydroxide distributed on the outer surface of and inside the  
3     micron-sized particles.

1           44.    The composition of claim 41, wherein the first polymeric material is  
2    poly(methylmethacrylate).

1           45.    The composition of claim 41, wherein the second polymeric material is a  
2    poly(hydroxyethylmethacrylate).

1           46.    The composition of claim 41, wherein the ratio of the polymeric bone substitute to  
2    the crosslinkable prepolymer is from about 1:20 to 20:1.

1           47.    The composition of claim 46, wherein the ratio of the polymeric bone substitute to  
2    the crosslinkable prepolymer is from about 1:2 to 2:1.

1           48.    The composition of claim 35, further comprising a therapeutic agent.

1           49.    A cured composition formed by curing a composition comprising a curable  
2    admixture of a polymeric bone substitute and a crosslinkable prepolymer wherein the  
3    crosslinkable prepolymer comprises

4           (A)    a linear polymer selected from the group consisting of linear, hydrophobic  
5    biodegradable polymers and linear non-degradable hydrophilic polymers; and

6           (B)    at least one monomer or macromer containing at least one free radical  
7    polymerizable group, wherein at least one of the monomers or macromers includes an anhydride  
8    linkage and a polymerizable group selected from the group consisting of acrylate or  
9    methacrylate.

1           50.    The cured composition of claim 49, wherein the polymeric bone substitute  
2    comprises porous micron-sized particles, each particle having a core layer of a first

3 biocompatible polymeric material and a coating of a second biocompatible polymeric material  
4 surrounding the core layer, wherein the second polymeric material is hydrophilic and different in  
5 composition from the first polymeric material.

1 51. The cured composition of claim 49, wherein at least 20% (w/w) of the cured  
2 composition biodegrades in from about 6 to 10 weeks.

1 52. The cured composition of claim 51, wherein at least 50% (w/w) of the cured  
2 composition biodegrades in from about 6 to 10 weeks.

1 53. The cured composition of claim 49, wherein at least 20% (w/w) of the cured  
2 composition biodegrades in from about 6 to 12 months.

1 54. The cured composition of claim 53, wherein at least 50% (w/w) of the cured  
2 composition biodegrades in from about 6 to 12 months.

1 55. A method of promoting bone generation comprising the steps of:

2 (A) applying to an area in need of such promotion a composition comprising a curable  
3 admixture of a polymeric bone substitute and a crosslinkable prepolymer wherein the  
4 crosslinkable prepolymer comprises

5 (i) a linear polymer selected from the group consisting of linear, hydrophobic  
6 biodegradable polymers and linear non-degradable hydrophilic polymers; and

7 (ii) at least one monomer or macromer containing at least one free radical  
8 polymerizable group, wherein at least one of the monomers or macromers includes an anhydride  
9 linkage and a polymerizable group selected from the group consisting of acrylate or  
10 methacrylate; and

11 (B) curing the composition.

1 56. A method of stabilizing a dental implant comprising the step of:

2 at least partially embedding a dental implant into a cured composition wherein

3 the cured composition is obtained by curing a curable admixture of a bone substitute and a

4 crosslinkable prepolymer, wherein the crosslinkable prepolymer comprises

5 (i) a linear polymer selected from the group consisting of linear, hydrophobic

6 biodegradable polymers and linear non-degradable hydrophilic polymers; and

7 (ii) at least one monomer or macromer containing at least one free radical

8 polymerizable group, wherein at least one of the monomers or macromers includes an anhydride

9 linkage and a polymerizable group selected from the group consisting of acrylate or

10 methacrylate.

1 57. The method of claim 56, wherein the dental implant is at least partially embedded

2 into the cured composition by the steps of :

3 (1) planting a dental implant into a bone and/or bone void;

4 (2) at least partially embedding the dental implant by applying a curable admixture

5 around the dental implant; and

6 (3) curing the curable admixture to form the cured composite.

1 58. The method of claim 56, wherein the dental implant is at least partially embedded

2 into the cured composition by the steps of:

3 (1) at least partially filling a bone void by applying a curable admixture;

4 (2) curing the curable admixture to form the cured composite; and

5 (3) planting a dental implant into the bone by at least partially embedding the dental  
6 implant into the cured composite.

1 60. A method of drug delivery comprising the steps of:

2 (A) applying to an area in need of drug delivery a composition comprising a curable  
3 admixture of a bone substitute and a crosslinkable prepolymer, and a therapeutic agent,  
4 wherein the crosslinkable prepolymer comprises

1        61.    A composition comprising a curable admixture of a polymeric bone substitute and  
2    a crosslinkable prepolymer,

3        wherein the crosslinkable prepolymer has at least two polymerizable terminal groups and  
4    a viscosity such that, at a temperature of 0° to 60°C, the crosslinkable prepolymer is deformable  
5    into a three-dimensional shape and crosslinkable.

1        62.    The composition of claim 61 wherein the polymeric bone substitute comprises  
2    porous micron-sized particles, each particle having a core layer of a first biocompatible  
3    polymeric material and a coating of a second biocompatible polymeric material surrounding the  
4    core layer, wherein the second polymeric material is hydrophilic and different in composition  
5    from the first polymeric material.

1        63.    The composition of claim 62, further comprising an initiator.

1        64.    The composition of claim 63, wherein the initiator is a photoinitiator.

1        65.    The composition of claim 62, wherein the crosslinkable prepolymer comprises a  
2    hydrophilic region.

1        66.    The composition of claim 62 wherein the crosslinkable prepolymer contains from  
2    1 to 100 repeating units.

1        67.    The composition of claim 62, wherein the crosslinkable prepolymer comprises at  
2    least one biodegradable region and at least one polymerization region.

1       68.    The composition of claim 65, wherein the hydrophilic region of the crosslinkable  
2    prepolymer is a polyethylene glycol or a copolymer of ethylene oxide and an alkylene oxide with  
3    a degree of polymerization is from 2 to 500.

1       69.    The composition of claim 62, wherein the crosslinkable prepolymer comprises a  
2    polyacetal sequence.

1       70.    The composition of claim 62, wherein the crosslinkable prepolymer is  
2       (A)    a polyester sequence formed by copolymerizing a mixture of lactone comonomers  
3    wherein no one of the lactone comonomers in the polyester sequence is present in an amount of  
4    more than 75 mole%;  
5       (B)    a polyorthoester sequence; or  
6       (C)    a combination of the polyester sequence and the polyorthoester sequence.

1       71.    The composition of claim 67, wherein the polymerizable region contains  
2    ethylenic, acetylenic unsaturation or both.

1       72.    The composition of claim 62, wherein the diameter of the micron-sized particles  
2    is from about 250 microns to about 900 microns.

1       73.    The composition of claim 62, wherein the polymeric bone substitute further  
2    comprising a quantity of calcium hydroxide distributed on the outer surface of and inside the  
3    micron-sized particles.

1       74.    The composition of claim 62, wherein the first polymeric material is  
2    poly(methylmethacrylate).

1           75.    The composition of claim 62, wherein the second polymeric material is a  
2 poly(hydroxyethylmethacrylate).

1           76.    The composition of claim 62, wherein the ratio of the polymeric bone substitute to  
2 the crosslinkable prepolymer is from about 1:20 to 20:1.

1           77.    The composition of claim 70, wherein the ratio of the polymeric bone substitute to  
2 the crosslinkable prepolymer is from about 1:2 to 2:1.

1           78.    The composition of claim 62, further comprising a therapeutic agent.

1           79.    A cured composition formed by curing a composition comprising a curable  
2 admixture of a polymeric bone substitute and a crosslinkable prepolymer,  
3           wherein the crosslinkable prepolymer has at least two polymerizable terminal groups and  
4 a viscosity such that, at a temperature of 0° to 60°C, the crosslinkable prepolymer is deformable  
5 into a three-dimensional shape and crosslinkable.

1           80.    The cured composition of claim 79, wherein the polymeric bone substitute  
2 comprises porous micron-sized particles, each particle having a core layer of a first  
3 biocompatible polymeric material and a coating of a second biocompatible polymeric material  
4 surrounding the core layer, wherein the second polymeric material is hydrophilic and different in  
5 composition from the first polymeric material.

1           81.    The cured composition of claim 79, wherein at least 20% (w/w) of the cured  
2 composition biodegrades in from about 6 to 10 weeks.

1           82.    The cured composition of claim 81, wherein at least 50% (w/w) of the cured  
2   composition biodegrades in from about 6 to 10 weeks.

1           83.    The cured composition of claim 79, wherein at least 20% (w/w) of the cured  
2   composition biodegrades in from about 6 to 12 months.

1           84.    The cured composition of claim 83, wherein at least 50% (w/w) of the cured  
2   composition biodegrades in from about 6 to 12 months.

1           85.    A method of promoting bone generation comprising the steps of:

2           (A)    applying to an area in need of such promotion a composition comprising a curable  
3   adixture of a polymeric bone substitute and a crosslinkable prepolymer,  
4         wherein the crosslinkable prepolymer has at least two polymerizable terminal groups and  
5   a viscosity such that, at a temperature of 0° to 60°C, the crosslinkable prepolymer is deformable  
6   into a three-dimensional shape and crosslinkable; and

7           (B)    curing the composition.

1           86.    A method of stabilizing a dental implant comprising the step of:

2                 at least partially embedding a dental implant into a cured composition wherein  
3   the cured composition is obtained by curing a curable admixture of a bone substitute and a  
4   crosslinkable prepolymer, wherein the crosslinkable prepolymer has at least two polymerizable  
5   terminal groups and a viscosity such that, at a temperature of 0° to 60°C, the crosslinkable  
6   prepolymer is deformable into a three-dimensional shape and crosslinkable.

7           87.    The method of claim 86, wherein the dental implant is at least partially embedded  
8   into the cured composition by the steps of :

- (1) planting a dental implant into a bone and/or bone void;
- (2) at least partially embedding the dental implant by applying a curable admixture to the dental implant; and
- (3) curing the curable admixture to form the cured composite.

88. The method of claim 86, wherein the dental implant is at least partially embedded

2 into the cured composition by the steps of:

- (1) at least partially filling a bone void by applying a curable admixture;
- (2) curing the curable admixture to form the cured composite; and
- (3) planting a dental implant into the bone by at least partially embedding the dental implant into the cured composite.

89. A method of preparing objects of desired shape and size comprising the step of:

2 curing in a mold a curable admixture of a bone substitute and a crosslinkable

3 prepolymer, wherein the crosslinkable prepolymer has at least two polymerizable terminal

4 groups and a viscosity such that, at a temperature of 0° to 60°C, the crosslinkable prepolymer is  
5 deformable into a three-dimensional shape.

1 90. A method of drug delivery comprising the steps of:

(A) applying to an area in need of drug delivery a composition comprising a curable admixture of a bone substitute and a crosslinkable prepolymer, and a therapeutic agent,

4 wherein the crosslinkable prepolymer has at least two polymerizable terminal groups and  
5 a viscosity such that, at a temperature of 0° to 60°C, the crosslinkable prepolymer is deformable  
6 into a three-dimensional shape and crosslinkable; and

7 (B) curing the composition.

1           91.    The composition of claim 1, further comprising either the oxidizing component or

2   the reducing component of a redox initiator system.

1           92.    The composition of claim 35, further comprising either the oxidizing component

2   or the reducing component of a redox initiator system.

1           93.    The composition of claim 61, further comprising either the oxidizing component

2   or the reducing component of a redox initiator system.

1           94.    A composition comprising a curable admixture of

2           (A)    a polymeric bone substitute;

3           (B)    a crosslinkable prepolymer, comprising an anhydride of

4           (i)     a monomer or oligomer of a diacid or multifunctional acid and

5           (ii)    a carboxylic acid molecule which includes a crosslinkable group, having

6   an unsaturated hydrocarbon moiety;

7           (C)    a photoinitiator; and

8           (D)    one or both parts of a redox system containing an oxidizing component and a

9   reducing component.

1           95.    A method of forming a cured composition comprising:

2           (A)    forming a curable admixture of

3           (i)     a polymeric bone substitute;

4           (ii)    a crosslinkable prepolymer comprising an anhydride of a monomer or

5   oligomer of a diacid or multifunctional acid and a carboxylic acid molecule which includes a

6   crosslinkable group having an unsaturated hydrocarbon moiety;

- (iii) a photoinitiator; and
- (iv) a redox system comprising an oxidizing component and a reducing

partially curing said admixture by the reaction of the two component of the redox

exposing the partially cured curable admixture to sufficient radiation to

size said partially cured curable admixture.

96. A composition comprising a curable admixture of

(A) a polymeric bone substitute;

(B) a crosslinkable prepolymer comprising

(i) a linear polymer selected from the group consisting of linear, hydrophobic  
degradable polymers and linear non-degradable hydrophilic polymers; and

(ii) at least one monomer or macromer containing at least one free radical  
polymerizable group, wherein at least one of the monomers or macromers includes an anhydride  
and a polymerizable group selected from the group consisting of acrylate or  
methacrylate;

(C) a photoinitiator; and

(D) one or both parts of a redox system containing an oxidizing component and a  
reducing component.

97. A method of forming a cured composition comprising:

(A) forming a curable admixture of

(i) a polymeric bone substitute;

(ii) a crosslinkable prepolymer comprising

(a) a linear polymer selected from the group consisting of linear, hydrophobic biodegradable polymers and linear non-degradable hydrophilic polymers; and

(b) at least one monomer or macromer containing at least one free radical polymerizable group, wherein at least one of the monomers or macromers includes an anhydride linkage and a polymerizable group selected from the group consisting of acrylate or methacrylate.

(iii) a photoinitiator; and

(iv) a redox system comprising an oxidizing component and a reducing

partially curing said admixture by the reaction of the two component of the redox

exposing the partially cured curable admixture to sufficient radiation to

ize said partially cured curable admixture.

1 98. A composition comprising a curable admixture of

2 (A) a polymeric bone substitute;

3 (B) a crosslinkable prepolymer, wherein the crosslinkable prepolymer has at least two

4 polymerizable terminal groups and a viscosity such that, at a temperature of 0° to 60°C, the

5 crosslinkable prepolymer is deformable into a three-dimensional shape and crosslinkable.

6 (i) a monomer or oligomer of a diacid or multifunctional acid and

7 (ii) a carboxylic acid molecule which includes a crosslinkable group, having

8 an unsaturated hydrocarbon moiety;

9 (C) a photoinitiator; and

10 (D) one or both parts of a redox system containing an oxidizing component and a  
11 reducing component.

1 99. A method of forming a cured composition comprising:

2 (A) forming a curable admixture of

3 (i) a polymeric bone substitute;

4 (ii) a crosslinkable prepolymer; wherein the crosslinkable prepolymer has at  
5 least two polymerizable terminal groups and a viscosity such that, at a temperature of 0° to 60°C,  
6 the crosslinkable prepolymer is deformable into a three-dimensional shape and crosslinkable.

7 (iii) a photoinitiator; and

8 (iv) a redox system comprising an oxidizing component and a reducing

9 component;

10 (B) partially curing said admixture by the reaction of the two component of the redox  
11 system; and

12 (C) exposing the partially cured curable admixture to sufficient radiation to  
13 photopolymerize said partially cured curable admixture.